

# Glycemic Control in Diabetic American Indians

## Longitudinal data from the Strong Heart Study

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**OBJECTIVE** — To describe glycemic control and identify correlates of elevated HbA<sub>1c</sub> levels in diabetic American Indians participating in the Strong Heart Study, which is a longitudinal study of cardiovascular disease in American Indians in Arizona, Oklahoma, South Dakota, and North Dakota.

**RESEARCH DESIGN AND METHODS** — This analysis is based on data from the baseline (1989–1992) and first follow-up (1994–1995) examinations of the Strong Heart Study. The 1,581 diabetic participants included in this analysis were aged 45–74 years at baseline, were diagnosed with diabetes before and at baseline, and had their HbA<sub>1c</sub> levels measured at follow-up. HbA<sub>1c</sub> was used as the index of glycemic control. Characteristics that may affect glycemic control were evaluated for cross-sectional and longitudinal relationships by analysis of covariance and multiple regression.

**RESULTS** — There was no significant difference between median HbA<sub>1c</sub> at baseline (8.4%) and at follow-up (8.5%). Sex, age (inversely), and insulin and oral hypoglycemic agent therapy were significantly related to HbA<sub>1c</sub> levels in both the cross-sectional and longitudinal analyses. Current smoking, prior use of alcohol, and duration of diabetes were significant only for the cross-sectional data. Baseline HbA<sub>1c</sub> significantly and positively predicted HbA<sub>1c</sub> levels at follow-up. Comparison of HbA<sub>1c</sub> by therapy type shows that insulin therapy produced a significant decrease in HbA<sub>1c</sub> between the baseline and follow-up examinations.

**CONCLUSIONS** — Glycemic control was poor among diabetic American Indians participating in the Strong Heart Study. Women, patients taking insulin or oral hypoglycemic agents, and younger individuals had the worst control of all the participants. Baseline HbA<sub>1c</sub>, and weight loss predicted worsening of control, whereas insulin therapy predicted improvement in control. Additional therapies and/or approaches are needed to improve glycemic control in this population.

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Poor glycemic control is associated with microvascular complications and, to a lesser extent, with cardiovascular disease (CVD) in patients with diabetes (1–3). These complications progress more rapidly in older individuals with diabetes than in

their younger counterparts for any given degree of hyperglycemia (4). The goal of treatment in type 2 diabetes should be near-normal glycemia, which can prevent or slow the progression of microvascular complications (e.g., eye, kidney, and nerve damage) and improve CVD-associated risk factors (e.g., hyperlipidemia, hypertension, and hyperinsulinemia or insulin resistance) (5,6).

American Indians have disproportionately high rates of diabetes and some diabetes complications compared with the general U.S. population (7,8). This study attempted to systematically assess the degree of glycemic control and to identify the factors related to control in this population so that appropriate health measures can be instituted. The data are derived from the Strong Heart Study, a longitudinal study of 4,549 American Indians in Arizona, Oklahoma, South Dakota, and North Dakota (9).

### RESEARCH DESIGN AND METHODS

The study design, survey methods, and laboratory techniques of the Strong Heart Study have been reported previously (9,10). Briefly, the population for the baseline Strong Heart Study included American Indians aged 45–74 years from July 1989 to January 1992 who were resident members of the following tribes: the Akimel O’odham, Pee Posh, and Tohono O’odham tribes of central Arizona in the Gila River, Salt River, and Ak-Chin communities; the seven tribes of southwestern Oklahoma (Apache, Caddo, Comanche, Delaware, Fort Sill Apache, Kiowa, and Wichita); the Oglala and Cheyenne River Sioux in South Dakota; and the Spirit Lake Tribe in the Fort Totten area of North Dakota. The study protocol was approved by the Indian Health Service Institutional Review Board, by the institutional review boards of the participating institutions, and by the participating American Indian communities.

The baseline examination (1989–1992) of the Strong Heart Study consisted of a personal interview, physical examination, and

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**Abbreviations:** ADA, American Diabetes Association; CVD, cardiovascular disease.

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

blood measurements (9,11). Follow-up examinations were performed between 1994 and 1995. All survey methods and procedures were similar to those used at the baseline examination.

Previously diagnosed diabetes was determined if the participant was taking insulin treatment, was taking oral hypoglycemic agents, or presented with a history of diabetes during the interview. World Health Organization criteria were used to diagnose diabetes at baseline and follow-up examinations (12,13). Diabetes was diagnosed if the participant had either a fasting blood glucose level  $\geq 140$  mg/dl or a 2-h blood glucose level  $\geq 200$  mg/dl and no history of diabetes according to a questionnaire. Individuals who were newly diagnosed with diabetes on the basis of an oral glucose tolerance test performed during the follow-up examination were not included in the analyses.

The analysis was based on data from participants who were diagnosed with diabetes before and at the baseline examination and whose HbA<sub>1c</sub> was measured at the follow-up examination. HbA<sub>1c</sub>, the index of glycemic control (dependent variable), was determined for all participants at both examinations by high-performance liquid chromatography (14). The principal independent variables of interest were center (Arizona, Oklahoma, and South/North Dakota), sex, diabetes duration, therapy type, level of education, annual household income, family size, American Indian heritage (determined by self-report), years lived on a reservation, fluency in the native language, cigarette smoking, alcohol use, obesity, waist circumference, and physical activity. Obesity criteria were approximately the 85th and 95th percentiles for men and women aged 20–29 years from the Second National Health and Nutrition Examination Survey (15).

The demographic characteristics of the participants are presented as medians and ranges (for nonnormally distributed variables) or as numbers and percentages (for categorical variables). Differences in HbA<sub>1c</sub> between baseline and follow-up were compared by using the paired Wilcoxon's rank-sum test. Glycemic control, which was classified according to current American Diabetes Association (ADA) guidelines as HbA<sub>1c</sub> levels <6 (excellent), 6–6.9 (good [ $< 7$  is the goal for HbA<sub>1c</sub> control]), 7–7.9 (fair), and  $\geq 8\%$  (poor) (16), was compared by using the  $\chi^2$  test. Differences by

center, sex, age, and therapy type were tested by using the  $\chi^2$  approximation. Analysis of covariance (17) was performed for both the cross-sectional (HbA<sub>1c</sub> and the independent variables all collected at the follow-up examination) and longitudinal (HbA<sub>1c</sub> measured at follow-up related to variables collected at the baseline examination) data for various characteristics adjusted for center, sex, age, and therapy type. Independent factors related to HbA<sub>1c</sub> were evaluated with the use of stepwise multiple regression for both the cross-sectional and longitudinal data. Because HbA<sub>1c</sub> had a skewed distribution, log-transformed values were used in the analysis. Statistical significance was defined as  $P < 0.05$ .

**RESULTS** — Of the 2,099 diabetic participants at the baseline examination, 518 did not have an HbA<sub>1c</sub> measurement at the follow-up examination (either because they had no follow-up examination, had a follow-up examination but no sample available for HbA<sub>1c</sub> measurement, or were deceased). Thus, the effective sample size for this analysis is 1,581. Three main demographic characteristics (center, sex, and age) were compared between participants whose HbA<sub>1c</sub> levels were measured and those whose HbA<sub>1c</sub> levels were not measured at the follow-up examination.

There were no statistical differences for center and age, and fewer men had a follow-up measurement than women (69 vs. 79%, respectively) ( $P < 0.001$ ).

Almost half of the 1,581 diabetic participants were from Arizona, and more than two-thirds were women (Table 1). The median age was 60 years (range 49–78), and the median duration of diabetes was 11.3 years. Modes of therapy at follow-up were insulin (33%), oral hypoglycemic agents (37%), insulin combined with oral hypoglycemic agents (4%), and diet alone (26%). Oral hypoglycemic agents used during the baseline and first follow-up examinations were the various types of sulfonylureas on the market at that time. Median HbA<sub>1c</sub> did not differ significantly between baseline and follow-up for participants diagnosed with diabetes before baseline (9.1 vs. 9.0%) but differed significantly for participants diagnosed with diabetes at baseline (5.9 vs. 6.6%).

American Indians in Arizona had significantly higher median HbA<sub>1c</sub> levels ( $P < 0.01$ ) than participants at the other centers (Table 2). Women had poorer control than men, and HbA<sub>1c</sub> levels were inversely correlated with age. Patients taking insulin and/or oral hypoglycemic agents had poorer control and higher HbA<sub>1c</sub> levels than patients who used diet alone.

**Table 1—Demographic characteristics of participants: the Strong Heart Study**

Characteristics	Baseline	Follow-up
Center (n)	1,581	1,581
Arizona	765 (48)	765 (48)
Oklahoma	420 (27)	420 (27)
South Dakota and North Dakota	396 (25)	396 (25)
Sex (n)		
F	1,061 (67)	1,061 (67)
M	520 (33)	520 (33)
Age (years)	56 (45–74)	60 (49–78)
HbA <sub>1c</sub> (%) <sup>*</sup>		
Diagnosed before baseline <sup>†</sup>	9.1 (3.1–17.9)	9.0 (3.5–19.7)
Diagnosed at baseline <sup>‡</sup>	5.9 (4.0–14.8)	6.6 (4.0–19.1)
Total <sup>†</sup>	8.4 (3.0–17.9)	8.5 (3.5–19.7)
Duration of diabetes (years) <sup>§</sup>	7.0 (0–55)	11.3 (1.2–57.7)
Therapy type		
Insulin	394 (25)	520 (33)
Oral hypoglycemic agents	633 (40)	588 (37)
Insulin and oral hypoglycemic agents	20 (1)	60 (4)
Diet	534 (34)	413 (26)

Data are medians (ranges) or n (%). <sup>\*</sup>A total of 94 participants with missing value for baseline HbA<sub>1c</sub>; <sup>†</sup> $P > 0.05$  for comparison of HbA<sub>1c</sub> between baseline and follow-up; <sup>‡</sup> $P < 0.01$  for comparison of HbA<sub>1c</sub> between baseline and follow-up; <sup>§</sup> $P < 0.001$  for comparison of HbA<sub>1c</sub> between baseline and follow-up.

Table 2—Glycemic control status by center, sex, age-group, and therapy type

	HbA <sub>1c</sub> (%)				Median (range)
	<6	6–6.9	7–7.9	≥8	
Center					
Arizona	110 (14)	96 (13)	106 (14)	453 (59)	8.9 (3.5–16.1)
Oklahoma	79 (19)	60 (14)	73 (17)	208 (50)	8.0 (4.0–19.3)
South and North Dakota	74 (18)	55 (14)	58 (15)	209 (53)	8.3 (3.9–19.7)
P			0.05		<0.01
Sex					
F	156 (15)	143 (13)	155 (15)	607 (57)	8.7 (3.6–19.7)
M	107 (21)	68 (13)	82 (16)	263 (51)	8.1 (3.5–17.6)
P			<0.05		<0.01
Age-group (years)					
49–58	113 (16)	71 (10)	86 (12)	447 (62)	9.0 (3.5–16.1)
59–68	86 (15)	79 (14)	96 (16)	316 (55)	8.4 (3.9–19.3)
69–78	64 (23)	61 (21)	55 (19)	107 (37)	7.4 (3.6–19.7)
P			<0.01		<0.001
Therapy type					
Insulin*	29 (5)	57 (10)	87 (15)	407 (70)	9.3 (3.9–19.1)
Oral hypoglycemic agents	65 (11)	78 (13)	102 (18)	343 (58)	8.7 (3.5–19.7)
Diet	169 (41)	76 (18)	48 (12)	120 (29)	6.4 (3.6–14.8)
P			<0.01		<0.001

Data are medians (ranges) or n (%). \*Includes insulin combined with oral agents.

Relationships between the different variables and HbA<sub>1c</sub> levels (adjusted for center, sex, age, and therapy type) were evaluated for cross-sectional associations by using data in the follow-up examination and were evaluated as predictors from baseline to follow-up (Table 3). For the cross-sectional data, family size, years on a reservation, cigarette smoking, obesity (inversely), and duration of diabetes were significantly correlated with HbA<sub>1c</sub>, but only family size, years on a reservation, weight loss (inversely), and baseline HbA<sub>1c</sub> significantly predicted follow-up HbA<sub>1c</sub>.

The variables listed in Table 3, along with center, sex, age, and therapy type, were entered into the stepwise multiple regression models to identify significant cross-sectional and longitudinal influencing factors (Table 4). Sex, age (inversely), and oral hypoglycemic agent and insulin therapy were significantly related to high HbA<sub>1c</sub> levels in both the cross-sectional and longitudinal data. Current smoking, prior use of alcohol, BMI (inversely), and duration of diabetes were significant only for the cross-sectional data. Baseline HbA<sub>1c</sub> and weight loss were significantly and positively associated with follow-up HbA<sub>1c</sub> levels ( $P < 0.001$ ).

We further compared HbA<sub>1c</sub> levels at baseline and follow-up by therapy type. HbA<sub>1c</sub> levels for patients who received

insulin treatment decreased significantly at follow-up (median 9.8 vs. 9.3%, baseline vs. follow-up) ( $P < 0.001$ ); however, HbA<sub>1c</sub> levels for patients taking oral hypoglycemic agents (8.6 vs. 9.1%) ( $P < 0.05$ ) and using diet alone (5.9 vs. 6.1%) ( $P < 0.01$ ) significantly increased.

**CONCLUSIONS**— This is the first systematic analysis of glycemic control in a diverse group of American Indians in which the data collection methods and measures of HbA<sub>1c</sub> were identical for all groups of participants, which thereby allowed between-group comparisons. The data show that glycemic control was poor for the diabetic participants in all three geographical areas and exceeded the ADA guidelines, which suggest an HbA<sub>1c</sub> goal of <7% (16). A high proportion of individuals in all centers, both sexes, and all age-groups had HbA<sub>1c</sub> levels >8%. There was a higher rate of diabetes in Arizona (7), and glycemic control was somewhat worse in the Arizona communities, but the geographical differences were not statistically significant.

There were more women than men in our analysis. This reflects the higher death rates from CVD and accidents in men (18) and the higher prevalence of diabetes in women (7). Glycemic control, which was ascertained by higher HbA<sub>1c</sub> levels, was worse in women than in men. This sex dif-

ference was consistent both in the cross-sectional and longitudinal data. This is somewhat surprising because women are generally more inclined to seek health care and to comply with treatment regimens than men (19,20). Several factors may predispose diabetic women to difficulty with glycemic control. First, American Indian women with diabetes are more obese than men and may be more insulin resistant or have poorer pancreatic function. In addition, diabetes is known to affect women more adversely in several ways, including conferring a greater risk for CVD and exacerbating CVD risk factors (21).

Age was negatively correlated with HbA<sub>1c</sub>, and this relationship most likely reflects compliance with treatment. Several studies have shown that compliance with medical care increases with age (22–25), and better metabolic control is strongly associated with compliance with scheduled appointments as shown in other populations (26). No data on the frequency of compliance with medical care are available for this group. The rapid changes in the lifestyle of American Indians in each successive generation are accompanied by concomitant increases in risk factors for diabetes such as obesity and lack of physical activity (27–29). The poorer glycemic control in younger individuals may also reflect these changes.

In well-controlled clinical trials, weight loss has been shown to have a significant effect on improving glycemic control (30–32). In our observational sample, however, weight loss was positively related to HbA<sub>1c</sub> level. The fact that BMI was negatively correlated with HbA<sub>1c</sub> in the cross-sectional and longitudinal analyses most likely reflects weight loss from urinary glucose excretion that accompanies poor glycemic control in diabetes. This same disease process previously has been identified as leading to poor glycemic control (33,34). Weight loss has been shown to improve glycemic control in diabetic American Indians (35), and studies are needed to clearly define the extent that weight loss due to lifestyle changes versus hyperglycemia may affect glycemic control in American Indian populations.

Patients who were treated with insulin and oral hypoglycemic agents had significantly higher levels of HbA<sub>1c</sub> compared with patients treated with diet alone. This phenomenon has been observed in several studies (26,36,37) and may reflect the common clinical practice of placing

patients who have poor control on more aggressive therapies (26). Although insulin and oral hypoglycemic agent therapies were related to higher HbA<sub>1c</sub> levels than diet alone, longitudinal analysis showed that insulin-treated patients had a significant decrease in HbA<sub>1c</sub> levels over time. Conversely, significant increases in HbA<sub>1c</sub> levels were seen in patients treated with both oral hypoglycemic agents and diet therapy. These findings suggest that insulin therapy may be most effective in improving glycemic control in this population. If glycemic control remains poor with noninsulin therapies, insulin use should be considered. Although the proportion of diabetic patients taking insulin as a sole therapeutic agent increased significantly from 25% at baseline to 33% at the 4-year follow-up, the proportion of patients taking insulin was still lower in this population than the proportion of diabetic persons taking insulin in other populations (38).

Cigarette smoking, alcohol use, and duration of diabetes were significant positive correlates of HbA<sub>1c</sub> levels in the cross-sectional data but were not significant predictors in the longitudinal data when using multiple regression analysis (Table 4). One cross-sectional study showed that smoking was associated with poorer glycemic control in patients with type 1 diabetes (39); another study indicated that number of cigarettes smoked per day significantly and positively correlated with HbA<sub>1c</sub> levels in nondiabetic men (40). Smoking has also been related to diabetes complications (39,41–43), and smoking cessation has been shown to lower HbA<sub>1c</sub> levels (44) and increase HDL cholesterol levels (45). For these and other reasons, diabetic patients should not smoke. Limited information is available regarding alcohol use and HbA<sub>1c</sub>; two studies of type 1 diabetes had contradictory results when comparing HbA<sub>1c</sub> levels and alcohol consumption (46,47). Because it predisposes diabetic individuals to the development of neuropathy (48,49) and may lead to hypoglycemic reactions (50), alcohol use also should be discouraged in populations with a high prevalence of diabetes.

Duration of diabetes was related to worsening glycemic control in the cross-sectional data. This may be because of declining insulin secretion and increasing insulin resistance as the disease progresses. In the longitudinal data, diabetes duration was not independently related to HbA<sub>1c</sub>, but the effect of diabetes duration may be reflected

**Table 3—Mean values of HbA<sub>1c</sub> by different characteristics, adjusted for center, sex, age, and therapy type**

Characteristics	Cross-sectional data			Longitudinal data		
	n	Mean	P	n	Mean	P
Education (years)*						
<8	425	8.2 (7.9–8.4)	NS	425	8.2 (7.9–8.4)	NS
8–12	819	8.3 (8.1–8.5)		819	8.3 (8.1–8.5)	
>12	331	8.2 (8.0–8.5)		331	8.2 (8.0–8.5)	
Family size*						
<5 children	774	8.1 (7.9–8.3)	<0.05	774	8.1 (7.9–8.3)	<0.05
≥5 children	792	8.4 (8.2–8.6)		792	8.4 (8.2–8.6)	
Annual household income (\$)						
<5,000	463	8.2 (8.0–8.5)	NS	447	8.1 (7.8–8.3)	NS
5,000–10,000	278	8.4 (8.1–8.7)		261	8.4 (8.1–8.7)	
≥10,000	433	8.3 (8.1–8.6)		487	8.2 (8.0–8.4)	
American Indian heritage (%)*#						
<75	158	7.9 (7.6–8.3)	NS	158	7.9 (7.6–8.3)	NS
75–99	139	8.5 (8.1–8.9)		139	8.5 (8.1–8.9)	
100	1,284	8.3 (8.1–8.4)		1,284	8.3 (8.1–8.4)	
Years on reservation*						
<40	321	8.0 (7.7–8.2)	<0.05	321	8.0 (7.7–8.2)	<0.05
≥40	1,257	8.3 (8.1–8.5)		1,257	8.3 (8.1–8.5)	
Native language spoken*						
Fluently	1,023	8.3 (8.1–8.5)	NS	1,023	8.3 (8.1–8.5)	NS
Not fluently	296	8.2 (7.9–8.5)		296	8.2 (7.9–8.5)	
Never spoken	262	8.1 (7.8–8.4)		262	8.1 (7.8–8.4)	
Cigarette smoking						
Never smoked	511	8.0 (7.8–8.3)	<0.01	593	8.2 (7.9–8.4)	NS
Former smoker	666	8.2 (8.0–8.4)		596	8.1 (7.9–8.4)	
Current smoker	355	8.6 (8.3–8.8)		391	8.5 (8.2–8.7)	
Alcohol use						
Never used	300	8.1 (7.8–8.4)	NS	305	8.2 (7.9–8.5)	NS
Former user	844	8.4 (8.2–8.6)		731	8.4 (8.2–8.6)	
Current user	416	8.1 (7.9–8.3)		545	8.1 (7.9–8.3)	
Obesity†						
Normal weight	381	8.5 (8.2–8.8)	<0.05	325	8.4 (8.1–8.7)	NS
Overweight	469	8.2 (8.0–8.4)		476	8.1 (7.9–8.4)	
Obese	722	8.1 (7.9–8.3)		771	8.2 (8.0–8.4)	
Waist circumference (cm)‡						
<100	370	8.4 (8.1–8.7)	NS	370	8.2 (8.0–8.5)	NS
100–117	824	8.2 (8.0–8.4)		821	8.3 (8.1–8.5)	
≥118	373	8.1 (7.8–8.4)		385	8.1 (7.9–8.4)	
Weight loss (kg)‡§						
<3	—	—	—	391	8.0 (7.7–8.2)	<0.01
3–5	—	—	—	779	8.3 (8.1–8.5)	
≥5	—	—	—	393	8.4 (8.2–8.7)	
Duration of diabetes (years)						
>10	792	8.7 (8.5–8.9)	<0.001	612	8.5 (8.3–8.7)	NS
≤10	641	8.2 (8.0–8.4)		564	8.5 (8.2–8.7)	
Baseline HbA <sub>1c</sub> (%)						
<6	—	—	—	267	6.7 (6.5–7.0)	<0.001
6–6.9	—	—	—	215	8.0 (7.7–8.2)	
7–7.9	—	—	—	202	7.9 (7.6–8.2)	
≥8	—	—	—	803	9.0 (8.8–9.2)	
Physical activity in past year¶						
Yes	—	—	—	433	8.4 (8.0–8.6)	NS
No	—	—	—	1,006	8.2 (8.0–8.4)	
Physical activity in past week¶						
Yes	—	—	—	332	8.5 (8.2–8.7)	NS
No	—	—	—	1,102	8.2 (8.0–8.4)	

Data are geometric means (95% CIs). Geometric means are reported because the HbA<sub>1c</sub> values are log-normal. The means are considerably higher when patients newly diagnosed with diabetes at baseline are excluded (see Table 1). \*Unchangeable variable at baseline and follow-up examinations; #self-reported; †normal weight, BMI <27.8 for men and <27.3 for women; overweight, BMI 27.8–31.09 for men and 27.3–32.29 for women; obese, BMI ≥31.1 for men and ≥32.3 for women; ‡25 and 75% quartiles as cutoff points; §baseline weight minus follow-up weight; ¶leisure physical activity not measured in the follow-up examination.

Table 4—Stepwise multiple regression analysis for influencing factors of HbA<sub>1c</sub>

Variables	Cross-sectional data ( $R^2 = 0.21$ )			Longitudinal data ( $R^2 = 0.29$ )		
	Coefficient	SE	P	Coefficient	SE	P
Sex (F vs. M)	0.0695	0.0164	<0.001	0.0356	0.0164	<0.05
Age (years)	-0.0065	0.001	<0.001	-0.0044	0.001	<0.001
Cigarette smoking (current smoker vs. never)	0.0577	0.0183	<0.01	—	—	—
Alcohol use (former user vs. never)	0.0409	0.0154	<0.01	—	—	—
BMI (kg/m <sup>2</sup> )	-0.0038	0.0013	<0.01	—	—	—
Therapy type						
Oral hypoglycemic agents vs. diet	0.1776	0.02	<0.001	0.1396	0.02	<0.001
Insulin* vs. diet	0.2098	0.0221	<.001	0.1789	0.0218	<0.001
Duration of diabetes (>10 vs. ≤10 years)	0.0828	0.0172	<0.001			
Baseline HbA <sub>1c</sub> (%)	—	—	—	0.0411	0.0035	<0.001
Weight loss (kg)†	—	—	—	0.0049	0.0011	<0.001

Log-transformed values were used in the analysis. \*Including insulin combined with oral hypoglycemic agents; †baseline weight minus follow-up weight.

by other variables such as baseline HbA<sub>1c</sub>. Because duration of diabetes was self-reported in the examinations, reporting bias may limit the analysis of the association. Furthermore, because HbA<sub>1c</sub> levels reflect the severity of diabetes, baseline HbA<sub>1c</sub> was not surprisingly a significant predictor of poor glycemic control.

The socioeconomic and lifestyle variables reflected by level of education, family size, annual household income, American Indian heritage, years on a reservation, and fluency in the native language were not significantly related to glycemic control in multiple regression analysis in either the cross-sectional or longitudinal analysis, although some univariate relationships were seen. The effects of socioeconomic and lifestyle variables on glycemic control may depend on health beliefs and compliance with medical care. Lack of major differences in health beliefs and level of compliance among participants with different socioeconomic and traditional lifestyle variables may limit the effect of these variables on glycemic control.

Although many reports indicate that individuals with type 2 diabetes who exercise regularly have decreased HbA<sub>1c</sub> or glucose levels (31,32,51), physical activity was not significantly related to HbA<sub>1c</sub> levels in our data. However, this study is limited by the use of self-reported physical activity data and by low activity levels in almost all participants (52). Physical activity levels were similarly low in men and women and

thus could not explain the sex difference regarding glycemic control.

The variables included in the multiple regression models only accounted for a small proportion of the variance in HbA<sub>1c</sub> ( $R^2 = 0.21$  for the cross-sectional data,  $R^2 = 0.29$  for the longitudinal data) (Table 4). Multiple regression coefficients were small for several variables; because of the large sample size, these variables were thus statistically but not clinically significant. Important factors that were not measured in this study, such as compliance with treatment and self-management activities that may influence glycemic control, must be the principal determinants of control in this population.

Our study demonstrates that glycemic control is poor in diabetic American Indians in the Strong Heart Study. The longitudinal data, based on a 4-year follow-up, indicate that sex (women vs. men), age (inversely), therapy type (insulin and oral hypoglycemic agents vs. diet), baseline HbA<sub>1c</sub>, and weight loss (positively) were significant and independent predictors of high levels of HbA<sub>1c</sub>. The study also suggests that insulin is the therapy most likely to improve glycemic control. However, this study was conducted before the advent of several newer agents for glycemic control that have been shown to have various metabolic actions. The effects of these newer agents on glycemic control in American Indians will be evaluated in the next Strong Heart Study follow-up examination.

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